I. AMENDMENTS

AMENDMENTS TO THE CLAIMS

Please enter the amendments to claims 1, 5, 9, 10, 11, 67, 68, 69, 79, 82, and 83, as shown below.

1. **(Currently amended)** A method for synthesizing an isoprenoid or an isoprenoid precursor via a mevalonate pathway in a host cell, wherein the method comprises:

i) culturing a transformed host cell in a suitable medium, wherein the transformed host cell is a prokaryote that does not normally synthesize isopentenyl pyrophosphate (IPP) through the mevalonate pathway, and wherein the host cell comprises one or more nucleic acids heterologous to the host cell, wherein the one or more heterologous nucleic acids comprises nucleotide sequences that encode two or more mevalonate pathway enzymes, wherein said two or more mevalonate pathway enzymes comprises an enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA **as the first step in the synthesis of the isoprenoid or isoprenoid precursor** and one or more additional mevalonate pathway enzymes selected from:

(a) an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA;

(b) an enzyme that converts HMG-CoA to mevalonate;

(c) an enzyme that phosphorylates mevalonate to mevalonate 5-phosphate;

(d) an enzyme that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and

(e) an enzyme that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate,

said culturing providing for production of the two or more enzymes, resulting in synthesis of said isoprenoid or isoprenoid precursor in a recoverable amount of at least about 1 mg/L; and

ii) recovering the produced isoprenoid or isoprenoid precursor.

2. (Previously presented) The method of claim 1, wherein the one or more heterologous nucleic acids is integrated into the chromosome of the host cell.

3. (Previously presented) The method of claim 1, wherein the one or more heterologous nucleic acids is contained in at least one extrachromosomal expression vector.

4. (Previously presented) The method of claim 3, wherein the one or more heterologous nucleic acids is present in a single expression vector.

5. (**Currently amended**) A method for synthesizing isopentenyl pyrophosphate (IPP) via a mevalonate pathway in a host microorganism, wherein the method comprises:

culturing a transformed host prokaryote microorganism that does not normally synthesize IPP through the mevalonate pathway in a suitable medium, the transformed host microorganism comprising a single extrachromosomal expression vector heterologous to the host microorganism that comprises the nucleotide sequence set forth in SEQ ID NO 7 or a fragment thereof encoding the enzymes in a mevalonate pathway; wherein the mevalonate pathway comprises:

(a) ~~condensing~~ an enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA;

(b) ~~condensing~~ an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA;

(c) ~~converting~~ an enzyme that converts HMG-CoA to mevalonate;

(d) ~~phosphorylating~~ an enzyme that phosphorylates mevalonate to mevalonate 5-phosphate;

(e) ~~converting~~ an enzyme that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and

(f) ~~converting~~ an enzyme that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate, said culturing providing for production of the enzymes, wherein said production of said enzymes results in production of IPP.

6. (Previously presented) The method of claim 3, wherein each of the one or more heterologous nucleic acids is contained within a separate expression vector.

7. (Previously presented) The method of claim 3, wherein at least two of the one or more heterologous nucleic acids are contained in a single expression vector.

8. (Previously presented) The method of claim 3, wherein the one or more heterologous nucleic acids is contained in two expression vectors.

9. **(Currently amended)** A method for synthesizing isopentenyl pyrophosphate (IPP) via a mevalonate pathway in a host microorganism, wherein the method comprises:

culturing a transformed host prokaryote microorganism that does not normally synthesize IPP through the mevalonate pathway in a suitable medium, the transformed host microorganism comprising two extrachromosomal expression vectors, wherein the first expression vector comprises the nucleotide sequence set forth in SEQ ID NO 8, and the second expression vector comprises the nucleotide sequence set forth in SEQ ID NO 9 or a fragment thereof, which sequences or fragments thereof from the two vectors are heterologous to the host microorganism and encode the enzymes in a mevalonate pathway; wherein the mevalonate pathway comprises:

(a) ~~condensing~~ an enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA;

(b) ~~condensing~~ an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA;

(c) ~~converting~~ an enzyme that converts HMG-CoA to mevalonate;

(d) ~~phosphorylating~~ an enzyme that phosphorylates mevalonate to mevalonate 5-phosphate;

(e) ~~converting~~ an enzyme that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and

(f) ~~converting~~ an enzyme that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate, said culturing providing for production of the enzymes, wherein said production of said enzymes results in production of IPP.

10. **(Currently amended)** A method for synthesizing isopentenyl pyrophosphate (IPP) via a mevalonate pathway in a host microorganism, the method comprising:

culturing a transformed host microorganism in a suitable medium, the transformed host microorganism comprising one or more nucleic acids heterologous to the host microorganism, wherein the host microorganism is a prokaryote that does not normally synthesize IPP through the mevalonate pathway, wherein the one or more nucleic acids comprises nucleotide sequences encoding two or more enzymes selected from:

a) an enzyme ~~capable of condensing~~ that condenses two molecules of acetyl-CoA to acetoacetyl-CoA, wherein said enzyme is from *Ralstonia*, *Saccharomyces*, or *Escherichia coli*, **wherein said enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA is present as the first step in the synthesis of the IPP**;

b) an enzyme ~~capable of condensing~~ that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA, wherein said enzyme is from *Blattella or Saccharomyces*;

c) an enzyme ~~capable of converting~~ that converts HMG-CoA to mevalonate, wherein said enzyme is from *Sulfolobus*, *Haloferax*, or *Saccharomyces*;

d) a *Saccharomyces* enzyme ~~capable of phosphorylating~~ that phosphorylates mevalonate to mevalonate 5-phosphate ;

c) a *Saccharomyces* enzyme ~~capable of converting~~ that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and

f) a *Saccharomyces* enzyme ~~capable of converting~~ that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate,

said culturing providing for production of the enzymes, wherein said production of said two or more enzymes results in production of IPP.

11. **(Currently amended)** A method for synthesizing isopentenyl pyrophosphate (IPP) via a mevalonate pathway in a host microorganism, the method comprising:

culturing a transformed host microorganism in a suitable medium, the transformed host microorganism comprising one or more nucleic acids heterologous to the host microorganism, wherein the host microorganism is a prokaryote that does not normally synthesize IPP through the mevalonate pathway, wherein the one or more heterologous nucleic acids comprises nucleotide sequences encoding two or more enzymes selected from:

a) an enzyme ~~capable of condensing~~ that condenses two molecules of acetyl-CoA to acetoacetyl-CoA encoded by the nucleotide sequence of SEQ ID NO 1**, wherein said enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA is present as the first step in the synthesis of the IPP**;

b) an enzyme ~~capable of condensing~~ that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA, encoded by the nucleotide sequence of SEQ ID NO 2;

c) an enzyme ~~capable of converting~~ that converts HMG-CoA to mevalonate encoded by the nucleotide sequence of SEQ ID NO 3;

d) a *Saccharomyces* enzyme ~~capable of phosphorylating~~ that phosphorylates mevalonate to mevalonate 5-phosphate encoded by the nucleotide sequence of SEQ ID NO 4;

e) a *Saccharomyces* enzyme ~~capable of converting~~ that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate encoded by the nucleotide sequence of SEQ ID NO 5; and

f) a *Saccharomyces* enzyme ~~capable of converting~~ that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate encoded by the nucleotide sequence of SEQ ID NO 6,

said culturing providing for production of the enzymes, wherein said production of said two or more enzymes results in production of IPP.

12. (Canceled)

13. (Previously presented) The method of claim 1, wherein the method further comprises reacting isopentenyl pyrophosphate with dimethylallyl pyrophosphate or a polyprenyl pyrophosphate in the presence of at least one enzyme to provide a polyprenyl pyrophosphate isoprenoid precursor.

14. (Previously presented) The method of claim 13, wherein the one or more heterologous nucleic acids further comprises:

g) a nucleic acid comprising a nucleotide sequence coding for an enzyme that converts isopentenyl pyrophosphate to dimethylallyl pyrophosphate.

15. (Previously presented) The method of claim 1, wherein the isoprenoid precursor is IPP, and wherein the IPP is further modified enzymatically by the action of isopentenyl pyrophosphate isomerase and one or more polyprenyl pyrophosphate synthases to provide an isoprenoid selected from the group consisting of a monoterpene, sesquiterpene, diterpene, sesterterpene, triterpene, tetraterpene, and a steroid.

16. (Original) The method of claim 15, wherein the isoprenoid is a monoterpene.

17. (Original) The method of claim 16, wherein the monoterpene is selected from the group consisting of limonene, citranellol, and geraniol.

18. (Original) The method of claim 15, wherein the isoprenoid is a sesquiterpene.

19. (Original) The method of claim 18, wherein the sesquiterpene is selected from the group consisting of periplanone B, artemisinin, ginkgolide B, forskolin, and farnesol.

20. (Previously presented) The method of claim 15, wherein the isoprenoid is a diterpene.

21. (Original) The method of claim 20, wherein the diterpene is selected from the group consisting of casbene and paclitaxel.

22. (Canceled)

23. (Previously presented) The method of claim 1, wherein the prokaryote is *Escherichia coli.*

24.-60. (Canceled)

61. (Previously presented) The method of claim 5, wherein the prokaryote is *Escherichia coli.*

62. (Previously presented) The method of claim 8, wherein the prokaryote is *Escherichia coli.*

63. (Previously presented) The method of claim 9, wherein the prokaryote is *Escherichia coli.*

64. (Previously presented) The method of claim 10, wherein the prokaryote is *Escherichia coli.*

65. (Previously presented) The method of claim 11, wherein the prokaryote is *Escherichia coli.*

66. (Previously presented) The method of claim 15, wherein the prokaryote is *Escherichia coli.*

67. (**Currently amended**) The method of claim 64, wherein the enzyme ~~capable of condensing~~ that condenses two molecules of acetyl-CoA to acetoacetyl-CoA is from ~~an~~ *E. coli* ~~enzyme~~.

68. (**Currently amended**) The method of claim 64, wherein the enzyme ~~capable of condensing~~ that condenses acetyl-CoA with acetoacetyl-CoA is [[a]] from *Saccharomyces* ~~enzyme~~.

69. (**Currently amended**) A method for synthesizing isopentenyl pyrophosphate (IPP) via a mevalonate pathway in a host microorganism, wherein the method comprises:

culturing a transformed host microorganism in a suitable medium, the transformed host microorganism comprising at least two operons heterologous to the host microorganism, wherein each of said two operons comprises nucleotide sequences encoding enzymes in the mevalonate pathway, and wherein the host microorganism is a prokaryote that does not normally synthesize IPP through the mevalonate pathway; wherein the mevalonate pathway comprises:

(a) ~~condensing~~ an enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA, **wherein said enzyme that condenses two molecules of acetyl-CoA to acetoacetyl-CoA is present as the first step in the synthesis of the IPP**;

(b) ~~condensing~~ an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA;

(c) ~~converting~~ an enzyme that converts HMG-CoA to mevalonate;

(d) ~~phosphorylating~~ an enzyme that phosphorylates mevalonate to mevalonate 5-phosphate;

(e) ~~converting~~ an enzyme that converts mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and

(f) ~~converting~~ an enzyme that converts mevalonate 5-pyrophosphate to isopentenyl pyrophosphate, said culturing providing for production of the enzymes,

wherein said production of said two or more enzymes results in production of IPP.

70. (Previously presented) The method of claim 69, wherein said at least two operons are contained in a single extrachromosomal expression vector.

71. (Previously presented) The method of claim 69, wherein at least one of said at least two operons is contained in a different extrachromosomal expression vector from another of said at least two operons.

72. (Previously presented) The method of claim 69, wherein at least one of said at least two operons is integrated into a chromosome of said transformed host microorganism.

73. (Previously presented) The method of claim 69, wherein said transformed host microorganism also comprises a heterologous nucleic acid comprising a nucleotide sequence encoding an enzyme that converts IPP to dimethylallyl pyrophosphate, and the method further comprises reacting the IPP with dimethylallyl pyrophosphate and a polyprenyl pyrophosphate synthase to provide a polyprenyl pyrophosphate isoprenoid precursor.

74. (Previously presented) The method of claim 69, wherein said transformed host microorganism is *E. coli*.

75. (Previously presented) The method of claim 70, wherein said transformed host microorganism is *E. coli*.

76. (Previously presented) The method of claim 71, wherein said transformed host microorganism is *E. coli*.

77. (Previously presented) The method of claim 72, wherein said transformed host microorganism is *E. coli*.

78. (Previously presented) The method of claim 74, wherein said *E. coli*. also produces IPP by a DXP pathway.

79. **(Currently amended)** The method of claim 74, wherein

a) said enzyme ~~capable of condensing~~ that condenses two molecules of acetyl-CoA to acetoacetyl-CoA is from *Ralstonia*, *Saccharomyces*, or *Escherichia coli*;

b) said enzyme ~~capable of condensing~~ that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA is from *Blattella or Saccharomyces*;

c) said enzyme ~~capable of converting~~ that converts HMG-CoA to mevalonate is from *Sulfolobus*, *Haloferax*, or *Saccharomyces*; and

d) said enzymes ~~capable of phosphorylating~~ that phosphorylate mevalonate to mevalonate 5-phosphate, ~~capable of converting~~ that convert mevalonate 5-phosphate to mevalonate 5-pyrophosphate, and ~~capable of converting~~ that convert mevalonate 5-pyrophosphate to isopentenyl pyrophosphate, are from *Saccharomyces*.

80. (Previously presented) The method of claim 74, wherein each of said at least two operons comprises a heterologous nucleic acid selected from the group consisting of:

a) the nucleotide sequence set forth in SEQ ID NO 1;

b) the nucleotide sequence set forth in SEQ ID NO 2;

c) the nucleotide sequence set forth in SEQ ID NO 3;

d) the nucleotide sequence set forth in SEQ ID NO 4;

e) the nucleotide sequence set forth in SEQ ID NO 5; and

f) the nucleotide sequence set forth in SEQ ID NO 6.

81. (Previously presented) The method of claim 76, wherein the first vector contains the nucleotide sequence set forth in SEQ ID NO:8 and the second vector contains the nucleotide sequence set forth in SEQ ID NO. 9.

82. **(Currently amended)** The method of claim 79, wherein the enzyme ~~capable of condensing~~ that condenses two molecules of acetyl-CoA to form acetoacetyl-CoA is [[an]] from *E. coli* ~~enzyme~~.

83. **(Currently amended)** The method of claim 79, wherein the enzyme ~~capable of condensing~~ that condenses acetyl-CoA to acetoacetyl-CoA to form HMG-CoA is [[a]] from *Saccharomyces* ~~enzyme~~.

84. (Previously presented) The method of claim 1, wherein the two or more enzymes are from at least two distinct organisms.

85. (Previously presented) The method of claim 1, wherein at least one of the two or more enzymes is from an organism other than *Saccharomyces cerevisiae*.

86. (Canceled)

87. (Previously presented) The method of claim 1, wherein the transformed host cell overproduces the isoprenoid or isoprenoid precursor by at least about 5 fold as compared to a control host cell that is not transformed with the one or more heterologous nucleic acids.

88. (Previously presented) The method of claim 1, wherein the one or more nucleic acids comprises nucleotide sequences encoding three enzymes in the mevalonate pathway.

89. (Previously presented) The method of claim 1, wherein the one or more nucleic acids comprises nucleotide sequences encoding four enzymes in the mevalonate pathway.

90. (Previously presented) The method of claim 1, wherein the one or more nucleic acids comprises nucleotide sequences encoding six enzymes in the mevalonate pathway.

91. (Previously presented) The method of claim 69, wherein the IPP is further modified enzymatically by the action of isopentenyl pyrophosphate isomerase to provide dimethylallyl pyrophosphate (DMAPP).

92. (Previously presented) The method of claim 91, wherein the DMAPP is further modified enzymatically with one or more polyprenyl pyrophosphate synthases to provide an isoprenoid.

93. (Previously presented) The method of claim 92, wherein the host microorganism produces the isoprenoid in a recoverable amount of at least about 1 mg/L.

94. (Previously presented) The method of claim 92, wherein the isoprenoid is a monoterpene.

95. (Previously presented) The method of claim 94, wherein the monoterpene is selected from limonene, citranellol, and geraniol.

96. (Previously presented) The method of claim 92, wherein the isoprenoid is a sesquiterpene.

97. (Previously presented) The method of claim 96, wherein the sesquiterpene is selected from periplanone B, artemisinin, ginkgolide B, forskolin, and farnesol.

98. (Previously presented) The method of claim 92, wherein the isoprenoid is a diterpene.

99. (Previously presented) The method of claim 98, wherein the diterpene is selected from casbene and paclitaxel.

100. (Previously presented) The method of claim 92, wherein the isoprenoid is a triterpene.

101. (Previously presented) The method of claim 92, wherein the isoprenoid is a tetraterpene.

102. (Previously presented) The method of claim 92, wherein the isoprenoid is a steroid.